

## ABSTRACT

Methods and compositions for performing RNA interference comprising a wide  
5 variety of stabilized polynucleotides suitable for use in serum-containing media and for *in vivo* applications, such as therapeutic applications, are provided. These polynucleotides permit effective and efficient applications of RNA interference to applications such as diagnostics and therapeutics through the use of one or more modifications including orthoesters, terminal conjugates, modified linkages and 2' modified nucleotides.

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